

## **REMARKS**

Claims 1-96 are under examination. Claims **1-11, 18-20, 32-38, 40-48, 53, 54** and **63-69** have been elected for prosecution. Claims 12-17, 21-31, 39, 49-52, 55-62 and 70-96 have been withdrawn as being drawn to non-elected inventions.

Claims 1, 3-11, 18, 19 and 20 have been amended. Claims 2, 40-48, 53, 54, and 63-69 have been cancelled.

### **Objections**

The abstract of the disclosure remains objected as not conveying structural makeup. Applicants have amended the specification by providing the Abstract that includes a formula and definition of the variables to more clearly inform the public of the chemical makeup of Applicants' compounds. Applicants respectfully request the objection be removed.

Claims **5, 11, 20** and **44** are objected under 37 CFR 1.75(c) as being improperly dependent from a previous claim. Applicants have amended claims **5, 11** and **20** and have cancelled claim **44**.

### **Rejections under 35 USC § 112 first paragraph**

Applicants acknowledge withdrawn of part of previous rejections under 35 USC § 112. Claims **33-36, 38, 40, 42-48, 53, 54** and **65-67** and **69** remain rejected under 35 USC § 112 first paragraph because the specification does not enable for the treatment of all forms of male and female sexual dysfunction.

The Office Action specifically cites an online publication, which reviews current treatments (and their mechanism of action) directed to erectile dysfunction. Most of the compounds, or class of compounds, discussed in said publication are those known to have local vasodilator effect (either by being vasodilators *per se* or by antagonizing a vasoconstriction). The present invention relates to the use of specific dopamine agonists acting selectively on D<sub>4</sub> dopamine receptors that are located in specific areas of the central nervous system. Dopamine was recognized as having erectogenic effects when disappointing secondary effects became evident in patients with Parkinson's disease

being treated with apomorphine. Apomorphine is a non-selective D2/D4 dopaminergic agonist and has been used to treat sexual dysfunction despite the liability of strong secondary emetic effects. The core of the present invention is the use of agonists that are selective for dopamine D4 subtype only located in specific areas of the CNS. As stated also in the online reference indicated by the Examiner, D4 receptors are located in areas of the brain strongly related to cognitive, behavioral and emotional function. It is also stated in said reference that dopamine receptors located in said specific brain areas are strongly implicated in sexual behavior and they may also be able to increase female sexual arousal.

Applicants respectfully reiterate that, the relevant law states that to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must teach one of skill in the art to make and use the invention without undue experimentation. This requirement can be satisfied by providing sufficient disclosure, either through illustrative examples or broad terminology. This clause does not require “a specific example of everything within the scope of a broad claim”. In re Anderson 176 USPQ 331, at 333 (CCPA 1973). The inquiry with respect to scope of enablement under 35 U.S.C. § 112, first paragraph is whether it would require undue experimentation to make and use the claimed invention. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The effect of the compounds of the present invention was tested in the rat penile erectile model, which is widely recognized as an effective model to test compounds that would affect sexual behavior in general. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw the rejection.

Applicants acknowledge withdrawn of rejections under 35 U.S.C. § 102(b)

Rejections under 35 U.S.C. § 103(a)

Claim 5 remains rejected under 35 U.S.C. § 103(a) as being unpatentable over Buzas (GB '523) in view of Buzas (GB'080). GB '523 teaches compounds wherein R<sub>1</sub> is allyl, R<sub>2</sub> is 4-fluorophenyl, R<sub>3</sub> is piperazinyl, R<sub>4</sub> is a pyridinyl radical and L is C<sub>3</sub> alkylene. GB '080 teaches for similar compounds wherein L is C1-C<sub>3</sub> alkylene and R<sub>4</sub> is

a phenyl or piperonyl radical. Examiner then asserts that species in claim 5 remain obvious variants.

To establish *prima facie* obviousness *a suggestion* to modify a primary reference to achieve the presently claimed invention and *a reasonable expectation of success* in making and using the modified procedure to obtain the compounds of the present application must identified from a source other than Applicants' own specification. Applicants have found and can demonstrate that the combination of **L** equal to **C2 alkylene** and **R<sub>4</sub>** equals to **pyridinyl** results in compounds highly selective for dopamine receptors of the D4 subtype. This unexpected result prompted Applicants to characterize the compounds of the present invention as unique compounds useful as specific D4 agonists, a property that the prior art compound(s) did not have. Under these standards, Applicants respectfully contend that Applicant's invention is not obvious over Buzas (GB '523) in view of Buzas (GB'080).

Claim 5 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Yevich *et al.* Applicants submit that in view of the amendment of claim 1, which limits the heteroaryl group (R<sub>4</sub>) to pyridyl, this rejection is moot.

#### Rejections under 35 USC § 112 second paragraph

Claims 2, 32-38 and 40, 63, 65-69 are rejected under 35 U.S.C. § 112 second paragraph as being indefinite for failing to point out and distinctly claim the subject matter which applicants regards as the invention. The Office Action indicates several claims to be duplicates as determined by the Examiner.

Applicants have cancelled duplicate claims 63, 40, 65, 66, 67, 68, and 69, in addition to other claims as indicated in the first paragraph on the Remarks section

#### Conclusions

Applicants trust that all objections and rejections presented in the Office Action have been adequately addressed. In view of the amendments and the aforementioned remarks, Applicants respectfully believe that the application is now in condition for allowance and respectfully request that the Examiner to withdraw all outstanding rejections and to pass this application to allowance.

Should the Examiner have any concerns regarding the above, he is respectfully requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,  
T. Kolasa, et al.

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